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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/158,120	09/21/1998	LESLIE SID JOHNSON	469201-367	3563

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EXAMINER
ROARK, JESSICA H

ART UNIT	PAPER NUMBER
1644	17

DATE MAILED: 03/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/158,120	Applicant(s) JOHNSON, LESLIE SID	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,7,10,13,21 and 22* is/are pending in the application.

4a) Of the above claim(s) *10,13 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 September 1998* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The Examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Jessica Roark, Art Unit 1644, Technology 1600.

2. Claim status:
Claims 5, 8-9, 11-12 and 14-20 have been canceled previously.
Claims 1-4, 6-7, 10, 13 and 21-22 *are pending.*

3. Given the previous restriction requirement (12/20/99, Paper No. 4), which is hereby reiterated; claims 10, 13 and 22 have been withdrawn from consideration by the Examiner under 37 CFR 1.142(b), as being drawn to a nonelected invention; the requirement having been traversed Paper No. 5.

Claims 1-4, 6-7and 21 *are under consideration in the instant application.*

4. The request filed on 12/10/01 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/158,120 is acceptable and a CPA has been established. An action on the CPA follows.

5. Applicant's arguments, filed 10/30/00, are again acknowledged. These arguments were addressed in Paper No. 13, mailed 1/16/01.

Given the absence of additional rebuttal to the outstanding rejections of record in Applicant's Request for CPA filed 12/10/01 (Paper No. 16); unless otherwise noted the rejections are maintained for the reasons of record in Paper Nos 9 and 13.

It is noted that new grounds of rejection are set forth herein.

6. Sequence compliance: The instant application appears to be in sequence compliance for patent applications containing nucleotide sequence and/or amino acid sequence disclosures.

However, Applicant is required to identify the nucleotide and amino acid sequences with SEQ. ID NOS wherever sequences occur in the specification, drawings, and claims, in order to full satisfy the requirements of 37 CFR 1.821 (d) (see also MPEP 2422.02-2422.03).

Sequences lacking sequence identifiers are found at least on page 17 at lines 4, 8, 11, 14, 17 and 20.

Applicant is reminded that if any of these sequences are not contained in the instant CRF and paper copy, a new CRF, Paper Copy and Statement are required.

7. Applicant's amendment of the specification to contain specific reference to the earlier filed application is acknowledged. However, the status of nonprovisional parent applications (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

8. The abstract of the invention is not descriptive. A new abstract not to exceed 150 words is required that is clearly indicative of the invention *to which the claims are directed.*

9. Formal drawings have been submitted which fail to comply with 37 CFR 1.84.
Please see the form PTO-948 previously provided as part of Paper No. 9.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

*Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.*

10. It is noted that an IDS does not appear to have been filed.

11. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

12. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP 608.01(o). Correction of the following is required:

Applicant is requested to identify the written support for claim 21, particularly the claimed limitation of comprises a framework region, "at least a portion of which" is human.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 2-4, 6-7 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21, 2-4 and 6-7 are ambiguous in that it is unclear what the antibody comprises.

First it is noted that it is unclear if both the light chain and heavy chain constant regions are human, since the instant claim could be interpreted to encompass an antibody in which either the heavy chain, the light chain, or both the heavy and light chain constant region is human.

Second, it is unclear if the claim as written encompasses an antibody which comprises a total of three complementarity determining regions, each of which is of murine origin; or an antibody in which each of the three complementarity determining regions of both the heavy and light chain variable regions (i.e., six CDRs total) are of murine origin.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. After further consideration, Applicant's argument with respect to adequate written support for instant claim 6 has been found convincing. The previous rejection of claim 6 under 35 USC 112, first paragraph, as lacking adequate written description is withdrawn.

17. Claims 2-4, 6-7 and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The specification as originally filed does not provide support for the invention as now claimed. *This is a New Matter rejection for the following reasons*:

Applicant's amendment of 9/21/98 adds claim 21 but does not asserts that no New Matter has been added and does not point to support for the newly added limitation *comprises a framework region, "at least a portion of which" is human.* The instant claims now recite limitations which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Obviousness is not the standard for the addition of new limitations to the disclosure as filed. It is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977). New Matter is a written description issue.

Applicant is required to cancel the New Matter in the response to this Office Action.
Alternatively, Applicant is invited to clearly point out the written support for the instant limitations.

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

19. Claims 1-4 and 21 stand rejected under 35 U.S.C. 102(a) as being clearly anticipated by Tempest et al. (Biotechnology, March 1991, vol 9, pages 266-271, of record) for the reasons of record originally set forth in Paper No. 9, mailed 4/26/00.

Given the absence of additional rebuttal to the outstanding rejections of record in Applicant's Request for CPA filed 12/10/01 (Paper No. 16); the rejections are maintained for the reasons of record in Paper Nos 9 and 13.

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. Claims 1-4, 6-7 and 21 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Tempest et al. (Biotechnology, March 1991, vol 9, pages 266-271, of record) in view of Beeler et al. (J. Virol. 1989; 63:2941-2950, of record) for the reasons of record set forth originally in Paper No. 9, mailed 4/26/00.

Given the absence of additional rebuttal to the outstanding rejections of record in Applicant's Request for CPA filed 12/10/01 (Paper No. 16); the rejections are maintained for the reasons of record in Paper Nos 9 and 13.

22. Claims 1-4, 6-7, and 21 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Jones et al. (Nature, 1986; 321:522-525, of record) in view of Beeler et al. (J. Virol. 1989; 63:2941-2950, of record) for the reasons of record set forth originally in Paper No. 9, mailed 4/26/00.

Given the absence of additional rebuttal to the outstanding rejections of record in Applicant's Request for CPA filed 12/10/01 (Paper No. 16); the rejections are maintained for the reasons of record in Paper Nos 9 and 13.

23. Claims 1-4, 6-7 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Queen et al. (U.S. Pat. No. 5,693,762) in view of Beeler et al. (J. Virol. 1989; 63:2941-2950, of record).

The claims are drawn to an antibody against respiratory syncytial virus (RSV) that comprises at least one complementarity determining region (CDR) of a murine monoclonal antibody against RSV; or that comprises a human constant region, framework regions at least a portion of which are human, and three (or possibly six, given the ambiguous wording) CDRs of murine origin, in particular from a neutralizing murine antibody against site A or site C of the RSV F protein.

Queen et al. teach a method of producing high affinity "humanized" immunoglobulins (antibodies) in which one or more CDR, and possibly additional amino acids from the framework region, are replaced by donor immunoglobulin sequences (see entire document, e.g., as summarized in the Abstract). Queen et al. provide detailed guidance as to how to select "acceptor" human immunoglobulin sequences and make the appropriate replacement of CDRs, and if necessary, certain residues in the framework regions, to produced a humanized antibody that retains the high affinity for antigen of the donor antibody (see entire document, especially the Summary of the Invention at columns 2-3). Queen et al. also teach that "humanization" of rodent antibodies, including mouse antibodies, is important to reduce their immunogenicity in humans, making them better therapeutic reagents (see entire document, e.g., columns 1-3 or column 16).

Queen also teaches humanization of anti-viral mouse antibodies (see especially columns 26-29 and 32-35). Queen teaches that it is important to humanize anti-viral antibodies in order to provide non-immunogenic, efficacious antibodies for therapy of human viral infections (see especially column 32 at line 66 thru column 33).

Queen et al. do not teach humanization of murine antibodies to RSV in general, or humanization of neutralizing antibodies against the A or C site RSV F protein in particular.

Beeler et al. have been discussed previously and teach the production of neutralizing murine monoclonal antibodies to the RSV F protein, including antibodies to antigenic site A and antigenic site C of the F protein (see entire document). Beeler et al. review the art recognized clinical importance of RSV as one of the most important causes of respiratory tract illness in children worldwide and the role of antibodies in providing protection against RSV infection (e.g., page 2941, first paragraph). Beeler et al. also teach that the immune response to the F protein is important for neutralization of heterologous viral strains, and that antigenic sites A and C are relatively stable (see especially introduction on page 2941 and Discussion on page 2948, first full paragraph).

Given the teachings of the references, it would have been obvious to the ordinary artisan at the time the invention was made to apply the humanization methodology taught by Queen et al. to the neutralizing murine antibodies to the RSV F protein taught by Beeler et al. One of ordinary skill in the art would have had a reasonable expectation of successfully producing antibodies against RSV that comprised at least one and preferably three CDRs from each of the heavy chain and light chain variable regions of the murine anti-RSV F protein site A or C antibodies taught by Beeler et al. given the detailed methodology for replacing CDRs and producing high affinity antibodies taught by Queen et al. Antibodies humanized according to the teachings of Queen et al. would have also comprised a human constant region and a heavy and light chain variable region that itself comprised a framework region at least a portion of which was human.

Both Queen et al. and Beeler et al. teach antibody neutralization of viruses, and Queen et al. teach that humanized antibodies are more effective and efficacious antibodies for therapy of humans. Thus the ordinary artisan at the time the invention was made would clearly have been motivated to modify the RSV neutralizing antibodies of Beeler et al. to provide therapeutic reagents against a clinically important virus. In particular, the ordinary artisan would have been motivated to select anti-RSV antibodies which bound antigenic sites A or C of the RSV F protein for modification according to the method of Queen et al. because Beeler et al. teach that these sites are antigenically stable among RSV virus types, and so antibodies to these sites would have offered the broadest applicability as therapeutic agents for neutralization of RSV.

Given the teachings of antibodies having specificity for sites A and C of the RSV F protein, methods for introducing at least one and preferably three CDRs from the heavy and light chain variable regions of these antibodies into human antibody sequences, methods for transferring other murine framework residues as needed to result in high affinity humanized antibodies (a framework at least a portion of which is human), and a clear motivation for making these changes to the mouse antibodies so that they could more effectively be used a therapeutic agents; the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

24. It is again acknowledged that Applicant filed a Terminal Disclaimer on 10/30/00 (Paper No. 12) disclaiming the terminal portion of any patent granted on the instant application which is subsequent to the expiration date of U.S. Patent No. 5,824,307.

25. No claim is allowed.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
March 5, 2002

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
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3/5/02